Science in Singapore:

Aiming High for Biomedical Research

After 22 years at NCI, Nancy Jenkins, Ph.D., and Neal Copeland, Ph.D., left the Mouse Cancer Genetics Program they built at CCR to start a new adventure halfway around the world in Singapore's Institute of Molecular and Cell Biology (IMCB). In Singapore, the husband-and-wife team saw a unique opportunity to shape a new and exciting research enterprise in a region of the world they had both enjoyed so often as visitors. Although they were recruited to co-direct the Division of Genomics and Genetics, Copeland became the Executive Director of the Institute within a year. The IMCB is now part of a complex known as Biopolis, which includes several institutes that are conceptually similar to divisions of the NIH intramural program. However, the campus also houses the research and development operations of several pharmaceutical companies as well as fosters nascent biotechnology companies—an innovation that Jenkins and Copeland enthusiastically support for the perspective and talent it brings to translational research. The genetic models of cancer they created while at NCI and the insights derived from them have been widely recognized as seminal contributions to the field and were recognized and honored this year by the couple's election to the U.S. National Academy of Sciences.

A New Beginning

Our institute—the IMCB—is the oldest in Biopolis. It was founded in 1987, which doesn't sound that old until you consider that it is exactly half as old as the independent country of Singapore itself. In fact, it was only in the 1980s that Singapore attained the kind of economic prosperity that could support a strong research enterprise; however, the current enthusiasm and support for scientific research and development is remarkable. There is a definite feeling in the air that Asian science is on the rise, and those countries that can afford it—like Singapore—are pinning their economic future to scientific innovation. They are investing heavily, recruiting outstanding people, and giving them great resources.

The Nobel prize-winning developmental biologist Sydney Brenner, Ph.D., was instrumental in advising the government of Singapore to build the IMCB as a means to further basic science research and training. It was patterned originally after the Laboratory of Molecular Biology in Cambridge, U.K., one of Brenner's professional homes, which remains a special place today in no small part because—like the NIH—they have had "hard" funding directly from the government with which to recruit and support the best people.

Funding for the IMCB comes directly from Singapore's Ministry of Trade

(Photo: Courtesy of N. Copeland and N. Jenkins)

Nancy Jenkins, Ph.D. *(left)* and Neal Copeland, Ph.D. *(right)* continue their innovative cancer research at the Institute of Molecular and Cell Biology in Singapore.

and Industry. The institute comprises approximately 400 people in 30 labs implementing a range of basic research programs in cell biology, structural genetics, bacteriology, infectious disease, and of course cancer. The IMCB has a strong infrastructure for research in model organisms, including the largest zebra fish facility in South East Asia with approximately 9,000 fish tanks. Organizationally, the institute is divided into four divisions: Genomics and Genetics, Genes and Development, Systems Biology, and Cancer and Developmental Cell Biology, each headed by a deputy director. The divisions are actually a relatively recent invention, implemented by the previous Executive Director, Sir David Lane, who found a monolithic structure increasingly cumbersome as the institute grew in size. The directors are responsible for dispersing funds to investigators who are all on three- to five- year contracts. We make decisions about whether contracts will be renewed and the levels of funding each laboratory will receive in conjunction with an international scientific advisory board that helps us to review the progress and potential of our laboratories.

A Growing Biopolis

In 2004, the IMCB moved from its original home at the National University of Singapore to the newly constructed Biopolis campus. Still in its first phase of development, Biopolis currently has nine buildings. Next door to our institute is the Genome Institute started by Edison Liu, M.D., who also moved from CCR where he served as Clinical Director. In addition, Biopolis includes recently formed institutes in the areas of bioinformatics, nanotechnology, immunology, and medical biology.

The massive infusion of funding for Biopolis is, in part, tied to a strategy designed to attract pharmaceutical research and development. Singapore is already a major place for pharmaceutical manufacturing, but the goal is to create a rich environment for innovation as well as production. Biopolis provides space for pharmaceutical companies, which includes access to all of the core facilities (for a fee, of course); about half the space is currently occupied by companies including Eli Lilly and Company, Schering-Plough, Novartis, and GlaxoSmithKline. The Singapore government also supports nascent biotechnology companies that spin off research developed in the country.

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In short, Biopolis is a place that is striving to fuse basic science and translation without adhering to traditional fire lines separating academic and private research. When it comes, its success in fostering truly collaborative translational research will rest not only on this physical juxtaposition but also on changes that we see occurring in the pharmaceutical industry itself. The old bunker mentality of huge, secretive in-house research facilities seems to be giving way to a much more open and interactive mode of operation in which pharmaceutical companies are increasingly seeking out academic collaborators and partners. Everyone is realizing that the science needed to support successful drug development, from making the best compounds to developing the best assays, is too complex to go it alone.

Our Ongoing Research

For all of the changes we have seen in the last few years, one thing that hasn't changed for us is the direction of and vision for our own laboratory's research program. Right before we left NCI, we developed a new technology that allows us to induce many different cancers in mice. Previously, our focus had been on the hematopoietic cancers that we could produce using retroviruses and insertional mutagenesis, but we always felt limited because we were not able to study the solid cancers that are so much more common in people. Then we developed a technique that uses a transposon called Sleeping Beauty (SB)—a piece of DNA isolated from salmon that can be introduced into mouse genomes and mobilized so that it jumps from where it was originally inserted into another random part of the genome. If it disrupts one of the mouse genes and induces cancer in the process of re-insertion, we can quickly clone the gene responsible because the transposon also serves as a molecular tag. It is an incredibly powerful technology, and we can not only mobilize the transposon in all cells, but we can also selectively mobilize it in specific tissues and thereby model different organ tumors. Through this technology, we have set up many cancer models and also sent these mice to laboratories around the world for collaborations. The technology is still new, and we are working on ways to improve it. Our goal is to identify not only cancer genes but also new drug targets for human cancers—work we hope to do in partnership with the pharmaceutical companies that have come to Singapore.

In fact, there are very few places in the world apart from CCR where we could continue our life's work. And the NIH intramural program is really the only place we could have begun it. We could never have written enough grants to do all of the preliminary work that led to our transposon system. The project involved a sustained commitment of large-scale resources and high-risk science over the course of many years. At one point, we had 9,000 cages of mice in our facility in Frederick, and this scale was absolutely necessary to making the discoveries that we did.

An Evolving Institute

As we think about the future of the IMCB, we want to ensure that, like NCI, it is a place where investigators can think big and take risks. Singapore is continuing to invest heavily in science, and Biopolis is growing every day, but billions of dollars have also gone into new research programs for the universities. How do we distinguish our unique strengths? One way—although not the only way—is to focus on large interdisciplinary projects that are difficult to do in the university research environments where research funding is largely structured around individual investigator-initiated programs. Another method is to aim high at the kind of translational research that academia typically encounters difficulties in trying to achieve. In any case, the goals of the IMCB as it matures will reflect the development of Biopolis and of science across Singapore and South East Asia. It's an amazing, dynamic place to be.